Economic evaluation of duloxetine as a first-line treatment for painful diabetic peripheral neuropathy in Mexico
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The objective was to evaluate the cost-effectiveness of duloxetine as a first treatment for adults with diabetic peripheral neuropathy and moderate-to-severe pain. The authors concluded that duloxetine was a cost-effective intervention, in Mexico. Overall, the study was adequate and the reporting was sufficient. The authors’ conclusions reflect the results obtained, but the uncertainty present should be considered.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to evaluate the cost-effectiveness of duloxetine as a first treatment for adults diagnosed with diabetic peripheral neuropathy, with moderate-to-severe pain.

Interventions
The interventions were duloxetine, 60mg once daily; pregabalin 150mg, twice daily; branded gabapentin 60mg, three times daily; and generic gabapentin 60mg, three times daily.

Location/setting
Mexico/out-patient care.

Methods
Analytical approach:
A decision-tree model was used to map the clinical pathways and assess the costs and outcomes for the four interventions. The time horizon was 12 weeks. The authors reported that the perspective was that of the Mexican public health care system.

Effectiveness data:
The clinical and effectiveness data were from published studies. The main estimate of effectiveness was the extent of pain relief offered by each of the four drugs. A search of MEDLINE was undertaken to identify relevant articles evaluating treatment effectiveness. Only randomised controlled trials of patients with diabetic neuropathy were included. A total of 14 trials were found. The placebo arms of the 14 trials were pooled to estimate the baseline risk. The pooled relative risks (treatment versus placebo) for each of the four treatments, were derived using the relevant subsets of the 14 trials. These two estimates were combined to produce the placebo-adjusted relative risks for the model.

Monetary benefit and utility valuations:
The utility estimates were from a published systematic review of the burden of neuropathic pain, which identified three studies that assessed the utilities, by pain severity, in patients with diabetic neuropathy. Simple averages were calculated for the three pain states (mild, moderate and severe). A weighted average of the means for moderate and severe was used to estimate the baseline utility value for a poor outcome. For a good outcome, the utility was assumed to be the simple average, from the three studies, for those with mild pain. Adverse effects were assigned a 5% disutility for tolerable effects, or a 10% disutility for intolerable effects.
Measure of benefit:
Good pain relief and quality-adjusted life-years (QALYs) were the summary benefit measures. Good pain relief was defined as a patient subjective report of moderate pain relief or better; or much improved or better on the Patient Global Impression of Change scale.

Cost data:
The direct costs were those of the acquisition of the drugs, the management of adverse events, and poor pain relief. The drug costs used the average wholesale prices, for the medications, paid by government health care institutions. The health care costs were from the Mexican Institute of Social Security. The price year was 2010 and all costs were reported in Mexican pesos (MXN).

Analysis of uncertainty:
One-way sensitivity analyses were undertaken, by varying all the model parameters, over plausible ranges of values; where possible the 95% confidence interval was used. The results of this analysis were presented in a Tornado diagram. A probabilistic sensitivity analysis was undertaken, by assigning parametric distributions to each model parameter; this analysis was performed with 1,000 simulations.

Results
For 1,000 patients, the number of patients with good pain relief was 470 with generic or branded gabapentin, 534 with duloxetine, and 511 with pregabalin. The QALYs gained were 120.9 with generic or branded gabapentin, 125.7 with duloxetine, and 123.8 with pregabalin.

The costs incurred were MXN 3,069,735 with generic gabapentin, MXN 5,303,382 with branded gabapentin, MXN 3,561,411 with duloxetine, and MXN 4,571,247 with pregabalin.

Branded gabapentin was dominated by the other three interventions, as it was more costly and less or equally effective.

Compared with generic gabapentin, duloxetine was associated with an incremental cost of MXN 7,647 per additional patient with good pain relief, or MXN 102,433 per QALY gained. Pregabalin was associated with an incremental cost of MXN 36,712 per additional patient with good pain relief, or MXN 517,763 per QALY gained.

The probabilistic sensitivity analysis showed that at a willingness-to-pay threshold of the gross domestic product (GDP) per capita of Mexico, the likelihood that duloxetine was cost-effective was similar to that for generic gabapentin. If the threshold was three times the Mexican GDP per capita, the likelihood that duloxetine was cost-effective was 61%.

Authors’ conclusions
The authors concluded that duloxetine was a cost-effective intervention to manage painful diabetic peripheral neuropathy, in Mexico.

CRD commentary
Interventions:
The interventions were described, with appropriate details. It was not clear whether other treatments were relevant or would be relevant in other settings.

Effectiveness/benefits:
The authors reported that a systematic review was undertaken to identify the estimates for treatment effectiveness, but only one database, MEDLINE, was searched, and it is possible that relevant studies were not identified. Adequate details of the review were provided, including the inclusion and exclusion criteria, key search terms, and the methods used to combine the study data. Only limited information on the utilities was provided, and it was not clear how they were measured, but they appear to have been from the correct population. The use of placebo-adjusted relative risks may have been warranted, but this means that the baseline and relative risks were calculated using the same placebo data, making these data correlated. It was unclear whether this had an impact on the results, but it introduced uncertainty.

Costs:
The perspective was reported and it appears that all the major relevant costs were analysed. The sources for the costs were reported. Discounting was not necessary, given the short time horizon. The time horizon, price year and currency were all reported, but it was unclear if, given the chronic nature of the condition, the time horizon was sufficient to fully capture all of the costs and outcomes of the treatments.

Analysis and results:
A decision-tree model was used to synthesise the cost and outcome information. Appropriate details of the model structure, and a diagram, were provided. Exhaustive one-way and probabilistic sensitivity analyses were appropriately undertaken to assess the impact of uncertainty on the models’ results. The results were sufficiently reported. The authors stated that the main limitation of their study was the short time horizon.

Concluding remarks:
The placebo-adjusted relative risk introduced some uncertainty into the results, but its impact is difficult to fully assess. Overall, the study was adequate and the reporting was sufficient. The conclusions reflect the results obtained, but the uncertainty should be considered.

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